Stem-Cell Therapy

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Facing death inspires desperate measures. Like having your stem cells drawn in Florida, sent to Israel for processing, and shot into your ailing heart in the Dominican Republic. How far would you go to save your own life?

By Mark Cohen, Photographs by Mauricio Alejo. Posted March 6, 2010.

Ron O'Leary, 36, has never felt so exposed. Naked from the waist down, the 6'2", 210-pound man is lying atop an x-ray table, shivering in the air-conditioned chill. His blue eyes are fixed on the flexible 4-foot catheter about to be threaded through his femoral artery to his heart. He's flown 1,000 miles from his home in Florida to the Dominican Republic because parts of his heart are dead.

Now, an ECG broadcasts the plodding clunk-clunk of his scarred heart, which is pumping at 30 percent of its normal capacity. The nurses begin slathering his privates with a dark-brown antiseptic solution. Thoughts flit through his mind.

1. What is an ECG?

Boy, is that cold . . . Is this going to hurt? . . . I just want my heart back . . .

It's 2 p.m. in the dimly lit fourth-floor cardiovascular department at Centro de Otorrino, a private hospital in downtown Santo Domingo. O'Leary suffers from *idiopathic dilated cardiomyopathy*, a condition in which the heart muscle has stretched and then becomes weak and starts dying off. His heart is so damaged that it struggles to pump blood to his lungs, leaving the former restaurant owner unable to work and barely able to walk 40 yards without wheezing. His doctors in Florida counselled him that he needed to adjust to this new reality and prepare himself for a heart transplant in a few years if his condition deteriorated. Faced with this dramatic decline in his quality of life, O'Leary, who had been in good health 11 months prior, has flown to one of the poorest countries in the Caribbean for a new type of cardiac therapy. Doctors are going to use O'Leary's own stem cells to repair his heart. There's only *un problemita*. It's not legal, at least in the United States, because the U.S. Food and Drug Administration classifies the adult stem cell as a high-risk biologic product, and requires a rigorous review of its safety and effectiveness before it can be marketed. Prior to leaving home, O'Leary had signed 12 pages of waivers exempting the doctors who would be inserting the catheter from any kind of malpractice suit.

2. What is a catheter?

As a nurse places a sheet over O'Leary's groin, Dominican cardiologist Roberto Fernandez de Castro, M.D., picks up a polypropylene syringe from a stainless-steel surgical tray and gives it a slight shake. Inside, suspended in a yellow slurry of plasma, are 95 million of O'Leary's stem cells. They were grown from his own blood, which was extracted a week earlier at the offices of Regenocyte, the Naples, Florida-based company overseeing this procedure.

Next, Dr. Fernandez screws this small syringe into the opening of a foot-long black plastic syringe. It's then attached to the specially designed catheter that his partner, Hector Rosario, M.D., has begun feeding through a spot on O'Leary's upper-right thigh, up into the lower-left chamber of his heart. On the black-and-white fluoroscopy monitor, the catheter snakes into view. Its tip flicking in and out in response to Dr. Rosario's touch, the needle probes for a fertile site on the interior wall of O'Leary's left ventricle. Dr. Rosario turns a dial at the end of the syringe to lengthen the tip, and with the help of a plunger, implants the stem cells directly into O'Leary's heart.

"Ouch . . . pain, definitely a little pain there," says O'Leary.

On the ECG, O'Leary's rhythm spikes into a pattern of rapid squiggles. Dr. Fernandez mutters under his

breath in Spanish, and Dr. Rosario adjusts his grip on the needle. "That's actually a good sign," says Dr. Rosario. In his broken English, he explains that the pain shows there's enough healthy tissue in the heart muscle to react to being jabbed, which should help the stem cells take root and start growing new blood vessels. Then he maneuvers the needle to a second spot on the ventricle wall and fires off another 3 million cells.

Despite all the billion-dollar research, medical advances, and new life-extending recommendations of the past 50 years, there still isn't much you can do for a damaged heart. If you suffer a severe heart attack or an enlarged heart like O'Leary's, your choices are limited: Downshift your daily life so that watering the garden ranks as your most strenuous activity, or get in line with the other 3,000 Americans waiting for one of the 2,200 donor hearts available annually. The human heart may be one of our most mechanically sophisticated organs, but it's just not a good healer. With its own electrical system and unique muscle tissue beating 100,000 times a day, the heart is just too complex and too busy to repair itself significantly. Deprive critical cardiac tissue of oxygen, even for just a few minutes, and it dies. Weaken a single chamber or a single valve, and pumping efficiency plummets. Allow the damaged parts to dip below a certain baseline level of functioning, and they only become worse, never better.

Which is why stem-cell therapy is so intriguing—and potentially so lucrative. If science could harness the regenerative powers of the patients' own stem cells to reverse that slide, the savings in terms of lives and dollars would be enormous. It's nothing short of the groundbreaking first step on the path toward growing your own replacement heart. "Stem-cell therapy shifts the whole paradigm for treating heart disease, whether it's caused by heart attack, arrhythmia, or cardiomyopathy," says Joshua Hare, M.D., a cardiologist and the director of the University of Miami's interdisciplinary stem-cell institute. "My prediction is that in 10 to 15 years, thanks to this new ability to repair damage, heart disease will no longer be the number one killer in the country."

3. Heart disease is the “number one killer”in the United States. What are the #2 and #3 killers?

Since Regenocyte began offering treatments in the Dominican Republic in February 2008, its doctors have performed 75 of what it calls myocardial cellular regeneration procedures, at a cost of $64,500 a pop -- not a penny of which is covered by insurance. The process kicks off in Naples, Florida, with a blood draw; the blood is then immediately whisked by courier to the lab of Regenocyte's affiliate, TheraVitae, in Tel Aviv, Israel, for centrifuging and culturing. After a 5-day incubation period, which increases the stem cells' numbers a thousandfold, a TheraVitae representative boards a flight with the stem cells in a temperature-controlled tissue container, and arrives in Santo Domingo on the morning of the procedure. Shuttling cells back and forth across six time zones and performing the procedure outside the United States allows the company to operate without interference from U.S. authorities. The FDA's jurisdiction extends only to products manufactured within the United States; as it is, the only step of the process the company carries out on American soil is a needle stick to the arm.

Adult stem cells, like the ones used in this procedure, usually aren't associated with controversy. Embryonic stem cells, the kind grown from cryo-frozen fertilized eggs stored in liquid nitrogen in fertility clinics, are the ones that have been at the flash point of moral agonizing. The use of these cells to find cures for Parkinson's and Alzheimer's has been hotly debated in presidential elections, taken up by celebrity advocates like Michael J. Fox, and recently restarted by President Obama with the approval of the first cell lines available for research using federal funding. But something curious

happened while the ethics debates raged: The cardiac research community's enthusiasm for embryonic stem cells waned. "Many of us found the whole embryonic-cell debate to be overstated," says Dr. Hare. "The cells are unpredictable and have the tendency to turn cancerous. They're almost too powerful." So doctors began shifting their research to a more reliable and readily available type of stem cell. Like days-after-conception stem cells, adult stem cells can morph into virtually any other kind of cell, but they're found in the blood, bone marrow, and many organs of every living human. "Ten years ago, we didn't even think organs like the heart had stem cells or were capable of regeneration," says Dr. Hare. "We now realize that the body has a much greater capacity for rejuvenation. It just needs some help."

4. Why might embryonic stem cells be more prone to cancer than adult stem cells?

Like many of the estimated 300,000 American men under 55 suffering from some kind of cardiomyopathy, Ron O'Leary had next to no warning of the illness that would turn his high-functioning heart into a swollen lump of scar tissue. With his outgoing personality, mop of blond hair, and nose bent from an old football injury, he reminded people of a stocky Owen Wilson. Suddenly, in September 2007, he noticed his energy level dropping and had difficulty catching his breath during his long shifts at the restaurant. After several days, O'Leary went to a hospital emergency room, was told he had pneumonia, and left the ER clutching a prescription for an antibiotic. A week later he was coughing up blood and went to an ER at a second hospital. Doctors there ran an ECG and admitted him for additional tests.

The diagnosis: idiopathic dilated cardiomyopathy. The doctors couldn't even be sure what had caused O'Leary's heart condition, because it didn't run in his family. The most likely culprit was a viral infection. One doctor told O'Leary his was the weakest heart he'd ever seen. It was emptying just 8 percent of the blood that flowed into it before his doctors loaded him up with diuretics, beta-blockers, and ACE inhibitors, which boosted his ejection fraction to 30 percent.

"Numb. Just floored," O'Leary recalls of his reaction. "I mean, I'd never even really been sick before. The only medical professional I saw on a regular basis was my dental hygienist. My cardiologist put in a defibrillator, kept me on the medication, ordered regular tests, and told me I might eventually need a transplant." And under most circumstances, that would have been that. But O'Leary lives in Sarasota, close to the burgeoning South Florida stem-cell belt. After an article about his plight appeared in a local newspaper, O'Leary received an unsolicited call from a satisfied Regenocyte customer.

It's been 6 months since his stem-cell procedure, and Ron O'Leary answers the phone. He sounds out of breath. "Hey . . . How are you doing?" he says, his voice ragged and halting. "Sorry," he goes on. "I just got in from a bike ride." O'Leary, now 37, sounds to be settling back into his old routine. That is, his *old* old routine, the one he had before a freak-of-nature heart malady reduced him to puttering around like a geriatric.

A few weeks earlier, O'Leary traveled to Naples for his 6-month follow-up. His ejection fraction had increased to 44, which was 14 points above where it was before the doctors repaired parts of his heart. He didn't experience the 21-point jump that Regenocyte says is typical, but 14 points is a significant improvement.

For O'Leary, though, the most telling test may have been one he administered to himself a week before his office visit. He'd ventured out onto a local bike trail for a 20-mile ride with two friends. "It's not like I was racing Lance Armstrong; these guys are in their 50s," he says. "On the way back I took off for a stretch. I left them behind. That's when I knew. I feel like there's nothing I can't do."

How stem cells can repair your heart

To find out which of the stem-cell therapies being tested are the most promising, we surveyed key researchers. Here are their predictions.

If you suffer dilated cardiomyopathy Amit Patel, M.D., a researcher at the University of Utah, is overseeing a clinical trial that he expects will enter its final phase in July 2010. Patients have 200 million of their own cultured bone-marrow stem cells injected into their heart muscle through a catheter. The stem cells may secrete growth factors, and then other cells in the heart help out by remodeling scar tissue, growing new blood vessels, and boosting heart-muscle function.

If you survive a heart attack Jay Traverse, M.D., a cardiologist at the Minneapolis Heart Institute, is using bone-marrow-derived stem cells to treat people within 3 to 7 days of a heart attack. In his phase 1 and phase 2 clinical trials, doctors infuse 150 million stem cells into patients' hearts using a modified catheter. The stem cells may improve the efficiency of their hearts by growing new blood vessels.

If you have heart failure Joshua Hare, M.D., director of the interdisciplinary stem-cell institute at the University of Miami, is leading a phase 2 trial to treat heart- failure patients. The patients have 20 million to 200 million bone-marrow stem cells, either theirs or ones derived from a donor, put into their hearts through a catheter. The benefits are due to a combination of blood-vessel regeneration, new cardiac-tissue growth, and scar-tissue reduction.

If you have heart disease Douglas Losordo, M.D., director of cardiovascular regenerative medicine at Northwestern University, recently completed a phase 2 trial of patients suffering from chronic chest pain due to blocked arteries. Stem cells har vested from the patients' blood are injected into their hearts and arteries through a catheter. The stem cells improve bloodflow by stimulating the growth of new blood vessels and expanding the diameter of coronary arteries.

If you need a heart transplant Doris Taylor, Ph.D., director of the cardiovascular repair center at the University of Minnesota stem-cell institute, is using human heart stem cells to grow live hearts on cadaver scaffolds. The cadaver heart is stripped of cells and then stem and progenitor cells are introduced. A beating heart develops in about a week. She's working on animal studies and expects the first human implant trial to start in a few years.

5. When a drug company is testing a new drug, they divide the group of people that they're testing on into two smaller groups: one receives the actual drug, and the other receives a sugar-pill with no drug in it.

Why would they need to do this, to ensure that the drug works?
Do a wikipedia search for **Placebo Effect** to find out more.

6. If your heart was failing, would you consider this procedure? List at least two advantages and two disadvantages about the procedure as described in the article above.

7. In a paragraph (10 Sentences) explain the difference between **Adult Stem Cells** and **Embryonic Stem Cells**. You may want to talk about the ethical issues surrounding either of them.